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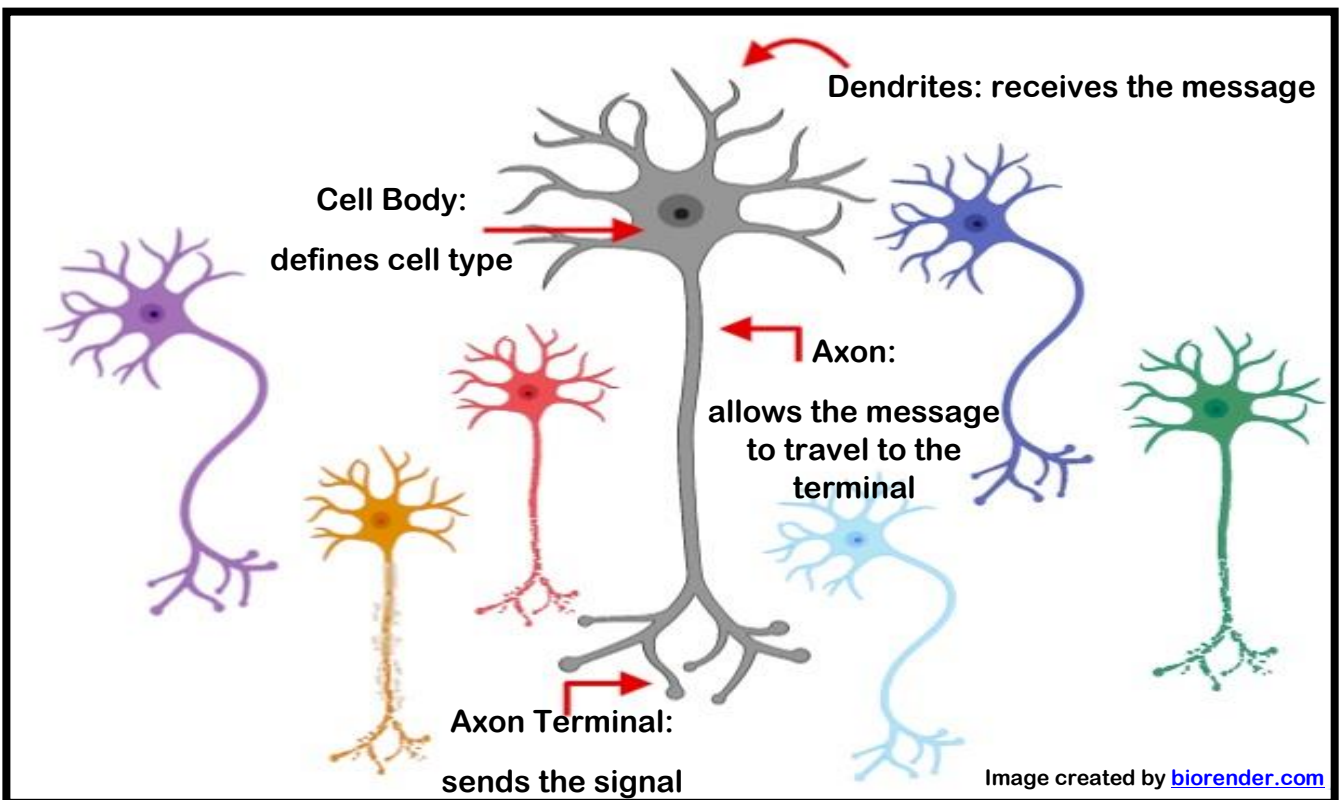
Message Received: Looking for the cells in the brain that receive pain signals from the bladder

By Michelle Valkanas

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Staff Article



There are millions of different types of neurons, all receiving different messages from your body.

Have you ever been stuck in traffic and had to pee so bad that you were sure that your bladder was going to explode? At that moment, all you could think about was the pain. Ironically, this discomfort was in an organ you only ever think about in times like this. Traffic finally breaks and you quickly find the nearest bathroom, and void your bladder. In that moment, you have never wanted anything more in your entire life, it is euphoric. Instantly, the pain goes away and you can go on ignoring your bladder again. How can this pain that is completely unbearable, go away in an instant?

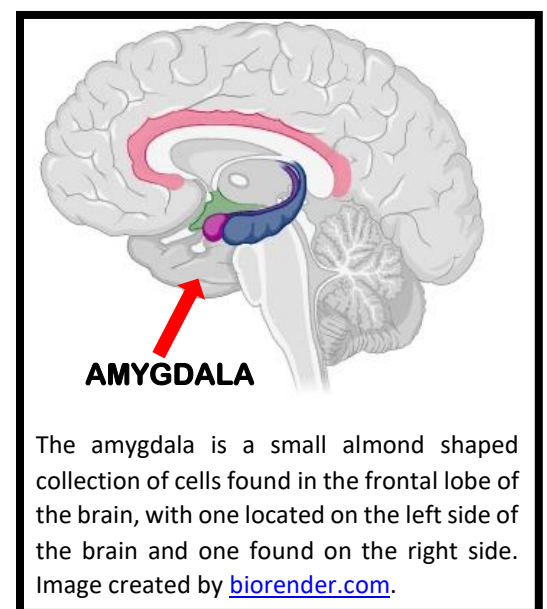
While this is a relatable story for many, some individuals never truly get that feeling of relief. It is estimated that there are 5-10 million people in the USA suffering from chronic bladder pain and other Urological Chronic Pelvic Pain Syndromes (UCPPS). Of these cases, 3-7 million of them are women (Berry et al., 2011).

Like other types of pain, bladder pain occurs when a message is sent from the bladder to the brain. The message is received, the brain responds, and a series of reactions occur. The response comes from neurons, which are nerve cells in the brain sending electrical signals through the spinal cord. There are close to 100 billion neurons in the brain and they are not all the same. Different neurons receive and respond to different messages. Additionally, there are millions of different cell types that could all be receiving the same message. This poses a challenge to scientists as they try to determine which neurons are receiving which messages, making treatment of things like migraines and bladder pain difficult.

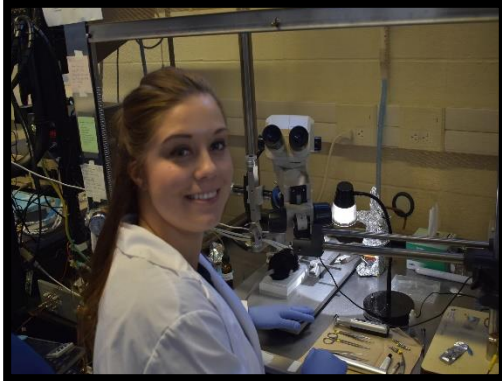
To make things even more complicated, in addition to the millions of cell types, *the right and left side of the brain process pain differently!* People commonly refer to themselves as being right-brained or left-brained, referring to whether they are creative and artistic (right) or analytical and methodical (left). This theory lumps the entire brain into left or right, but individual parts of the brain can also process things differently (right vs left).

This is the case for the tiny almond-shaped part of the brain called the amygdala. There are two amygdalae in your brain, you guessed it, one on the right and one on the left. The amygdala is most famous for playing a role in emotion, specifically fear, but it is becoming clear that it also plays a role in processing pain.

Dr. Benedict Kolber's lab at Duquesne University has in fact proven that the right side of the amygdala drives bladder pain, while the left side of the amygdala blocks bladder pain (Sadler et al., 2017). This allows researchers



in the Kolber lab to now focus their time on finding ways to specifically block pain-driving messages by targeting only the right side of the amygdala. Alternatively, they can try to increase pain-decreasing messages by targeting the left side of the amygdala.



Harley Bonar, 3rd year Ph.D. Candidate in the Kolber Lab, studying cell types in the brain that receive bladder pain messages.

Harley Bobnar is one of these researchers in the Kolber lab. Her work specifically focuses on how the brain receives the message of pain from the bladder. Bobnar, a 3rd year Ph.D. Candidate, measures the change in firing rates as a response to bladder pain. Firing rate refers to the electric charge, known as an action potential, traveling across the neurons in the brain. This works like a domino-effect where one charge leads to another charge, which leads to another. By tracking the cell types that “light up” with an electrical charge and which ones remain silent, scientists can identify the

cells involved in receiving and responding to the message of bladder pain. “I think the most exciting part of my research is identifying what specific cell types are influenced by bladder pain”, Bobnar states.

By understanding the cell types involved, scientists can begin developing treatments that target those specific cells. Bobnar emphasizes the importance of understanding how our brains specifically react to bladder pain. “If we can understand the underlining mechanisms... we could come up with better therapeutic approaches to treat the chronic condition” she states.

While this seems like a needle-in-a-haystack, the Kolber lab has already honed their focus in on a specific type of protein believed to be released during bladder pain, called *CGRP*. *CGRP*, calcitonin gene-related peptide, is a protein released in the brain and has been shown to play a role in receiving pain messages. *CGRP* is responsible for the pain felt during a migraine, and recent strides have been made in migraine treatment by blocking *CGRP* using monoclonal antibodies. The antibodies bind to the *CGRP* directly and/or to the cell that the *CGRP* binds to. This blocks any effects *CGRP* may have, therefore decreasing the pain caused by migraines.

The Kolber lab hopes to see similar treatments implemented for bladder pain in the future, but first the cell types involved must be uncovered. Bobnar, taking the Benjamin Franklin approach, forges forward, waiting for lightening to strike and the cell types involved to be revealed.

For more information on the research that the Kolber lab is currently working on, visit their website at:

<http://www.scienceresearch.duq.edu/bio/biofac/bkolber/research.html>.

Resources:

Berry, S.H., Elliott, M.N., Suttorp, M., Bogart, L.M., Stoto, M.A., Eggers, P. et al. (2011) Prevalence of symptoms of bladder pain syndrome/interstitial cystitis among adult females in the United States. *The Journal of urology* **186**: 540-544.

Sadler, K.E., McQuaid, N.A., Cox, A.C., Behun, M.N., Trouten, A.M., and Kolber, B.J. (2017) Divergent functions of the left and right central amygdala in visceral nociception. *Pain* **158**: 747.

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